

IN RE APPLICATION OF: MATTHEW T. SCHOLZ ET AL.

SERIAL NO: 08/855,933

FILED: MAY 14, 1997

FOR: BIOADHESIVE COMPOSITION AND PATCH

ASSISTANT COMMISSIONER FOR PATENTS  
WASHINGTON, D.C. 20231

Sir:

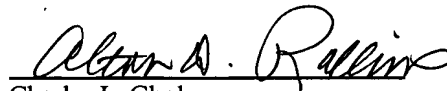
Transmitted herewith is an amendment in the above-identified application.

- ☐ No additional fee is required.
- ☐ Small entity status of this application under 37 C.F.R. §1.9 and §1.27 has been established by a verified statement previously submitted.
- ☐ Small entity status of this application under 37 C.F.R. §1.9 and §1.27 has been established by a verified statement submitted herewith.
- ☒ Additional documents filed herewith: 2nd Request for an Interference with PTO-850 and attachment, Request for Expedited Prosecution, and Petition for Extension of Time (1 month)

The Fee has been calculated as shown below:

	CLAIMS REMAINING AFTER		HIGHEST NUMBER PREVIOUSLY PAID FOR	NO. EXTRA CLAIMS	RATE	CALCULATIONS
TOTAL	26	MINUS	20	6	X \$ 22 =	\$132.00
INDEP	4	MINUS	3	1	X \$ 82 =	\$82.00
	MULTIPLE DEPENDENT CLAIMS				+ \$ 270 =	\$0.00
			TOTAL OF ABOVE CALCULATIONS =			\$214.00
	Reduction by 50% for filing by Small Entity					\$0.00
	Recordation of Assignment				+ \$ 40 =	\$0.00
	TOTAL					\$214.00

- ☒ A check in the amount of \$324.00 is attached.
- ☒ Please charge any additional Fees for the papers being filed herewith and for which no check is enclosed herewith, or credit any overpayment to deposit Account No. 15-0030. A duplicate copy of this sheet is enclosed.
- ☒ If these papers are not considered timely filed by the Patent and Trademark Office, then a petition is hereby made under 37 C.F.R. §1.136, and any additional fees required under 37 C.F.R. §1.136 for any necessary extension of time may be charged to Deposit Account No. 15-0030. A duplicate copy of this sheet is enclosed.

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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :

MATTHEW T. SCHOLZ ET AL. :

SERIAL NO: 08/855,933 :

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FOR: BIOADHESIVE COMPOSITION  
AND PATCH

ASSISTANT COMMISSIONER FOR PATENTS  
WASHINGTON, D.C. 20231

SIR:

AMENDMENT AND REQUEST FOR RECONSIDERATION UNDER 37 CFR 1.116

This amendment and request for reconsideration is responsive to the office action  
mailed July 02, 1998.

AMENDMENT

Please add the following new claims 145-150.

145. A method of achieving and/or maintaining a therapeutically effective blood  
level of a drug in a mammal, which method comprises the steps of:

(a) adhering to an oral mucosal surface of a mammal a

composition including an inert film backing and a bioadhesive on one surface

of said inert film backing, wherein the bioadhesive includes (i) a particulate

polymeric resin which is polymerized from monomers selected from the group

consisting of acrylic acid, itaconic acid, citraconic acid, and methacrylic acid

having at least about 55% by weight of carboxylic acid groups based on the

weight of the resin and which comprises less than about 20% by weight, based

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on the total weight of all monomers in the polymer, of ethylenically unsaturated comonomers; and which particulate polymeric resin is dispersed substantially throughout from about 20 parts to about 250 parts by weight of a hydrophobic elastomeric synthetic polymer component, based on 100 parts by weight of the particulate polymeric resin, said elastomeric synthetic polymer component being selected from the group consisting of a block styrene-butadiene-styrene copolymer, a block styrene-isoprene-styrene copolymer, a polyisobutylene, a polybutadiene, an isoprene rubber, a carboxy-functional polyisoprene, a hydroxy-functional polyisoprene, an acrylate elastomer, and a mixture of two or more of the foregoing; (ii) a therapeutically effective amount of a drug selected from the group consisting of heparin, digoxin, polypeptides, proteins, and mixtures thereof; and (iii) optionally, a penetration enhancing amount of a penetration enhancer; and

(b) allowing the composition to remain adhered to said oral mucosal surface of a mammal for a time sufficient to release enough of said drug so that a therapeutically effective blood level of drug is achieved and/or maintained.

146. A method according to claim 145 wherein the composition comprises an effective penetration enhancing amount of a penetration enhancer selected from the group consisting of sodium lauryl sulfate, cetyl pyridinium chloride, polysorbate 80, polyoxyethylene 9-lauryl ether, glyceryl monolaurate, oleic acid, sodium glycocholate, sodium taurocholate, and sodium tauro-24,25-dihydrofusidate.

147. A method according to claim 146 wherein said drug is selected from the group consisting of digoxin, heparin, a polypeptide drug, and a protein drug.

148. A method according to claim 147 wherein said penetration enhancer is selected from the group consisting of sodium glycocholate, sodium taurocholate, and sodium tauro-24,25-dihydrofusidate.

149. A method according to claim 145 wherein said drug is digoxin.

150. A method according to claim 148 wherein said drug is digoxin.

#### REQUEST FOR RECONSIDERATION

The claims presently in the application are claims 125-150.

Applicants acknowledge with appreciation the interview between applicants' representatives, Mr. Rollins and Ms. Howard, and Primary Examiner Kulkosky on September 04, 1998. During the interview, applicants' representatives pointed out that all of claims 125-144 are substantially copied from Hieber et al. patent No. 5,516,523 for purposes of interference. Applicants' representatives also pointed out that applicants' related application serial No. 456,021 has recently issued as patent No. 5,750,136 (hereinafter referred to as "the '136 patent"). The '136 patent matured from a twice removed continuation from application serial No. 842,222, filed February 26, 1992, and 607,863, filed November 01, 1990, which is a continuation-in-part of application serial Nos. 486,554, filed February 27, 1990, and 431,664, filed November 03, 1989. That is, the '136 patent has the same specification as the present application, which is a twice removed division of application serial No. 842,222.

The subject matter of the present application is limited to subject matter that was restricted from the application that matured into the '136 patent (i.e., claims 154-157), so there

are no double patenting problems for the claims of this divisional application with regard to the claims of the '136 patent.

The issuance of the '136 patent demonstrates the patentability of methods of achieving and/or maintaining a therapeutically effective blood level of a drug in a mammal by adhering to the oral mucosal surface of the mammal a patch including the drug in a bioadhesive on at least one surface of the patch and in which the bioadhesive includes specific polymeric resins which are combinations of hydrophilic and hydrophobic polymers. New claims 145-150 incorporate as the bioadhesive polymer component the same bioadhesive polymers found to be patentable over the prior art during the prosecution of the '136 patent and defined in claim 21 of that patent.

Although the Fankhauser et al. reference is not listed on the face of the '136 patent as a reference which was considered during the prosecution of the '136 patent, that reference contains no suggestion of the particular combination of hydrophilic and hydrophobic polymers required by claims 145-150. Although the polymer material in the adhesive layer of the reference can contain the same polyacrylic acid type of hydrophilic polymers (e.g., Carbopol 934P), those polymers are used in the reference in combination with an ethoxylated, non-ionic surfactant. That is, the reference adhesive does not contain a particulate hydrophilic polymer dispersed substantially throughout a hydrophobic elastomeric synthetic polymer as required by claims 145-150 and the claims of the '136 patent. Thus the bioadhesive layer of Fankhauser et al. does not contain a drug and/or penetration enhancer dispersed in a hydrophilic polymer which is itself dispersed substantially throughout a hydrophobic elastomeric synthetic polymer component. As applicants demonstrated in the '136 patent prosecution, applicants' particular bioadhesive

combination of hydrophilic and hydrophobic polymers results in sustained release of the medication, whereas a hydrophilic polymer alone does not.

Although the Fankhauser et al. reference does teach the optional use in the adhesive layer of penetration-assisting substances, it does not teach or suggest that those agents are particularly useful with large drug molecules such as peptides, proteins, or polysaccharides.

Inasmuch as the Fankhauser et al. reference does not teach or suggest applicants' novel and nonobvious combination of polymers in the bioadhesive layer, it does not suggest applicants' processes of claims 145-150. In re Hira, 535 F.2d 67, 190 USPQ 15 (CCPA 1976).

Although the Ennis et al. reference teaches that nasal solutions or sprays containing protein and peptide therapeutic agents have better bioavailability through the nasal membrane if they contain permeation enhancers such as bile salts, there is no suggestion in the reference that the same combination of penetration enhancers and therapeutic agents would be useful in bioadhesives applied to the oral mucosa. Thus, neither the Fankhauser et al. reference nor the Ennis et al. reference provides any motivation to combine the teachings of those two references. This argument is also applicable in connection with claims 125-144, which were substantially copied from the Heiber et al. patent. A similar argument was accepted as overcoming the prior art during the prosecution of the Heiber et al. patent.

New claims 145-150 clearly respond to the examiner's comments and suggestions made in the office action with regard to 35 USC 112.

For the foregoing reasons, it is believed that at least new claims 145-150 (1) clearly are patentable over the prior art and (2) clearly interfere with the claims of the Heiber et al. patent. Consequently, a new (second) 37 CFR 1.607 request for interference with the Heiber et al. patent

is being submitted with this amendment. It is emphasized in this regard that it is necessary only that at least one claim in the present application be considered to be allowable in order to initiate the interference. MPEP 2306 first sentence following the quotation of 37 CFR 1.606 ("An interference may be declared between an application and a patent if the application and patent are claiming the same patentable invention, and at least one of the applicant's claims to that invention are [sic: is] patentable to the applicant.").

Consequently, if the primary examiner finds that at least one claim in the present application is allowable to applicants, applicants request that the examiner (1) withdraw the finality of the rejection of July 02, 1998 and issue an office action suspending action pending consideration of the declaration of an interference and (2) initiate the interference by forwarding the appropriate PTO-850 papers to the board for declaration of the interference. Of course, if all of the pending claims are considered to be allowable, then a notice of allowability (but not a notice of allowance) should be issued instead of the notice withdrawing the finality of the rejection and suspending further action, after which the appropriate PTO-850 papers should be forwarded to the board.

As previously indicated, claims 125-144 were copied from the Heiber et al. reference for purposes of interference. The examiner indicated during the interview that he was not entirely persuaded that the scope of applicants' copied claims 125-144 is justified. However, applicants' disclosure is at least as descriptive and broadly enabling as the Heiber et al. disclosure. Applicants' disclosure at page 12 line 5 through page 13 line 21 is at least commensurate with the scope of the therapeutic agents disclosed by Heiber et al. The therapeutic agents specifically described by applicants include peptide hormones, protein products such as insulin (page 13 lines

3-8), and polysaccharides such as digoxin and heparin. Heparin and calcitonin are the only therapeutic agents used in the examples of the Heiber et al. patent. Heparin and digoxin, as well as morphine salts, are specifically included in the very limited list of preferred drugs at applicants' specification page 13 lines 19-21, and digoxin is used in the tests reported in Examples 2-4 at pages 25-27. Digoxin is a polysaccharide having a molecular weight of 780.92, which is well within the scope of claims 125-150 and the claims of the Heiber et al. patent..

During the prosecution of the Heiber et al. application that is the parent to the application that issued as the Heiber et al. patent, the Heiber et al. claims were rejected as being unpatentable over the combination of Longenecker et al. patent No. 4,994,439 and Inoue et al. patent No. 4,772,470. The Longenecker et al. patent, like the Ennis et al. reference applied against applicants' claims herein, teaches compositions and processes for the administration of aqueous solutions of protein or peptide drugs across nasal membranes using a combination of a bile salt or fusidate with a nonionic detergent as penetration enhancers. The Longenecker et al. patent, like the Ennis et al. reference, is limited to teachings regarding solutions useful as nasal sprays. The Inoue et al. patent teaches oral bandages having an adhesive layer containing various medications. The party Heiber et al.'s response (paper No. 3 filed October 25, 1993 in Heiber et al. application serial No. 08/027,508) to the rejection emphasized that the teachings of Longenecker et al. could not properly be combined with the teachings of Inoue et al. to yield the combination of a hydrophilic bioadhesive containing a protein or peptide drug and a bile salt enhancer. That argument was deemed by the examiner to rebut the rejection in the parent Heiber et al. application. The application that issued as the Heiber et al. patent from which applicants' claims 125-150 are substantially copied, cited (but did not apply) the Longenecker et al. and

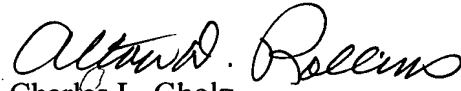
Inoue et al. patents. Thus, the examiner apparently relied on the prosecution history in the parent application to demonstrate patentability.

Thus, the rejections made against the claims of Heiber et al. are quite similar to the rejection of record against applicants' claims 125-144. If the Heiber et al. claims are patentable over the equivalent prior art that was applied against them, then applicants' claims 127-144 should be patentable to the applicants for the same reasons urged by Heiber et al. and summarized herein. Thus, the examiner is urged to review the prosecution history of the Heiber et al. parent patent in reconsidering the rejection of applicants' claims 125-144.

However, regardless of the patentability or unpatentability of claims 125-144, applicants' claims 145-150 are independently patentable based on the novel and nonobvious combination of hydrophilic and hydrophobic polymers in the adhesive layer.

A demonstration of support for the terms of the claims of new claims 145-150 in applicants' application is set forth in detail in the accompanying second 37 CFR 1.607 request, which is hereby incorporated by reference herein. The parts of the second request for interference relating to claims 125-144 are, of course, identical to the corresponding portions of the first request for interference.

Respectfully submitted,



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